

Attorney Docket No. P71338USO
Application No. 10/583,088

Remarks:

Claims 68, 70-76, 84, 86, 88, 89, and 91-106 are pending, with claims 72-75, 89, 92, 97, 99, 104 and 106 being withdrawn from consideration pursuant to restriction.

Claims 1-67, 69, 77-83, 85, 87, and 90 are cancelled, without prejudice or disclaimer.

Claim 68 is currently amended, essentially, by being rewritten as an independent claim, except that "SEQ ID NO: 5," recited in claim 67 (upon which previously presented claim 68 was dependent) is, now, included among the Markush group of which the claimed "oligonucleotide primer" is "consisting of." Claim dependencies are also changed, hereby, so as claims are not dependent on any newly cancelled claims. Other minor changes to the claims are effective, hereby, to more clearly define the invention.

Claims 67, 69, 83 and 85 were rejected under 35 U.S.C. §102(e) for allegedly being anticipated by U.S. 2003/0206887 (Morrissey). The rejected claims have been cancelled, rendering the rejection moot. Withdrawal of the rejection is in order.

Claims 67-71, 76-80, 83-86, 88, 90, 91, 93-96 and 98 were rejected under 35 U.S.C. §103(a) for allegedly being obvious over *J. Med. Virol.* 58, 325-331, 1999 (Saito), as allegedly evidenced by *Genome Res.*, 6, 986-994, 1996 (Heid), and GenBank sequence accession no. X98077, 1997 (GenBank sequence), *Liver*, 22, 374-379, 2002 (Higashi), *J. Virol.* 71, 5399-5407, 1997 (Stoll-Becker), *Clin. Cancer Res.*, 7, 2005-2015, 2001 (Su), and *Biotechniques*, 27, 528-536, 1999 (Buck). Reconsideration is requested, since the rejection constitutes clear error, both legally and factually.

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Clear error is manifest, first of all, by the rejection reliance on the unsupported finding (Office Action, page 17) (emphasis added): "Since the claimed primers simply represent structural homologs...derived from sequences suggested by the prior art...the claimed primers and probes are *prima facie* obvious over the cited references." Nothing of record—other than PTO allegations—supports the so-called structural homology represented by the presently claimed primers.

All the PTO can, and does, show—to support the alleged structural homology represented by the presently claimed primers—is some overlap between (1) the presently claimed sequences and (2) the prior art sequences. No evidence is put forward—only bare PTO allegations—that equates some sequence overlap with structurally homologous sequences, rendering the rejection fatally flawed. "The Examiner bears the initial burden...of presenting a *prima facie* case of unpatentability" and "the ultimate burden of persuasion on the issue," *In re Oetiker*, 24 USPQ2d 1443, 1444 and 1447 (Fed. Cir. 1992), which burden the "Examiner can satisfy...only by showing some objective teaching in the prior art," *Ex parte Obukowicz*, 27 USPQ2d 1063, 1065 (BPA&I 1992), and "the evidence upon which the examiner relies must clearly indicate that a worker of routine skill in this art would view the claimed invention as being obvious." *Ex parte Wolters*, 214 USPQ 735, 736 (BPA&I 1982) (emphasis added). "It is facts which must support the legal conclusion of obviousness," *Ex parte Crissy*, 201 USPQ 689, 695 (POBdApp 1976) (emphasis added), and the PTO "may not....resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in the factual basis. *In re Warner*, 154 USPQ 173, 178 (CCPA 1967) (emphasis original). An argument by the PTO "is not prior art." *In re Rijckaert*, 28 USPQ2d 1955, 1957 (Fed.

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Cir. 1993). Simply put, there is no evidence showing the differences between (1) the presently claimed sequences and (2) the prior art sequences—i.e., the non-overlapping sequences—are mere structurally homologous differences, as alleged in the rejection.

Moreover, mere overlap between the claimed subject matter and the prior art is insufficient to establish the obviousness of the claimed subject matter absent. *Ex Parte Wittpenn*, 16 USPQ2d 1730, 1731 (BPA&I 1990). As held by the Board, "the Examiner's conclusion lacks any logical foundation...[there being] no disclosure within the reference that would have led the routineer to make the critical selections to arrive at the claimed [subject matter]." 16 USPQ2d at 1731.

Similarly here, as in *Wittpenn* (16 USPQ2d at 1731), the rejection cites "no disclosure within the reference that would have led the routineer to make the critical [sequence] selection [from Saito] to arrive at the claimed [sequences]." Accordingly, "in the absence of some motivation to select" the presently claimed sequences, "the Examiner's conclusion lacks any logical foundation" and, so, "the rejection...cannot be sustained." *Wittpenn*, 16 USPQ2d at 1731. See *In re Baird*, 29 USPQ2d 1550 (Fed. Cir. 1994) ("The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious"). See also *In re Belle*, 26 USPQ2d 1529 (Fed. Cir. 1993), and *In re Jones*, 21 USPQ2d 1941 (Fed. Cir. 1992).

Clear error is also manifest by the rejection relying on "it would have been *prima facie* obvious to one of ordinary skill in the art...to have used the sequences, of the HBV genome to design primers and probes for the detection of the genome with a high expectation of success" (emphasis added, page 16 of the Office Action). Even assuming, arguendo, the prior art provided

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a high expectation of successful functionality, as alleged in the rejection, the "high expectation of success" falls short of the mark.

It is not pertinent whether the prior art device possesses the functional characteristics of the claimed invention if the reference does not describe or suggest its structure.

In re Mills, 16 USPQ2d 1430, 1433 (Fed. Cir. 1990). See *In re Swinehart*, 169 USPQ 226 (CCPA 1971). As explained above, all that the PTO can rely on in the cited prior art—to describe or suggest structure of the presently claimed sequences—is some sequence overlap; which overlap, "in the absence of some motivation to select" the presently claimed sequences, "lacks any logical foundation." *Wittpenn*, 16 USPQ2d at 1731.

Clear error is manifest, with all due respect, in the PTO reliance on the Supreme Court decision *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398 (2007). As set forth in the statement of rejection, itself (Office Action, page 7), "in [a] case where there is a limited number of possibilities, 'obvious to try' is obvious" under *KSR*. However, no such limited number of possibilities exists in the present case. Even taking as correct the 285 possible primers (i.e., "95 control primers...represent 1/3 of all possible primers") alleged in the statement of rejection (Office Action, page 18), 285 is hardly the limited number of possibilities envisioned by the Supreme Court in *KSR*.

Moreover, with all due respect, the rejection reliance on *In re Kubin*, no. 2009-1184, slip op. April 3, 2009, is misplaced, since *Kubin* is not in point. The rejection devotes about two full pages of text to repeating (apparently verbatim) the reasoning set forth by the *Kubin* court in affirming a §103 rejection in which "the record shows repeatedly that [prior art] Valiante's Example 12

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produces...the claimed polynucleotide" (*Kubin*, slip op. page 8) (emphasis added). As opposed to the facts in *Kubin*, and as admitted in instant rejection, itself (Office Action, page 16) (emphasis added), prior art "Saito et al. do not teach primers...[even] comprising...SEQ ID NO: 2, 3 or 8," let alone "consisting of SEQ ID NO: 2, 3 or 8," as presently claimed, rendering the rejection untenable. *In re Thrift*, 63 USPQ2d 2002, 2008 (Fed. Cir. 2002) ("a ground of rejection is simply inadequate on its face...[when] the cited references do not support each limitation of [each] claim").

Furthermore, even taking everything in the rejection as correct, *arguendo*, the rejection is overcome. That is, "the absence of secondary considerations," upon which relies "the claimed primers...[being] *prima facie* obvious over the cited references" (Office Action, page 17), is remedied by the Rule 132 declaration of the inventor, Marie-Phillippe Biron, provided herewith. As explained in the Rule 132 declaration (and precied below) the presently claimed oligonucleotide sequences exhibit surprising and unexpected results.

The Rule 132 declaration reports and discusses data obtained in tests comparing each of the primers of sequence SEQ ID NO: 2 and SEQ ID NO:3, according to the presently claimed invention, with structurally close primers—named "Sequence 2a" and "Sequence 3a" in the Rule 132 declaration—described in the international patent application WO 93/13120, of record (cited in the International Search Report of PCT/IB 2004/004022). As set forth in the declaration (paragraph bridging pages 6 and 7), the "Sequence 2a" and "Sequence 3a" are even closer to the presently claimed sequences than those found in the cited references.

Based on the data obtained, the Rule 132 declaration (pages 4 and 6) concludes, *i.a.*,

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The sequences SEQ ID NO: 2 and Sequence 2a are...both complementary sequences of the HBV genome and they hybridize to a single common region on the genome of HBV. However, SEQ ID NO: 2 has unexpected and advantageous properties compared to Sequence 2a...Given the results obtained with Sequence 3a, it is completely unexpected that SEQ ID NO: 3 is suitable for real-time PCR. SEQ ID NO: 3 has therefore unexpected properties.

Additionally, the Rule 132 declaration shows, contrary to the PTO finding, any primer of any length complementary to any segment of the HBV genome is not suitable for sensitive detection of hepatitis B viruses of several genotypes and, moreover, small changes in the primer nucleotide sequence can significantly affect sensitivity. As set forth in the Rule 132 declaration, itself (page 6), based on the data obtained,

a primer including the sequence of another primer while being complementary to the genome to be amplified, may lead to different and less advantageous amplification results. Thus, two sequences close to each other do not have intrinsically the same properties.

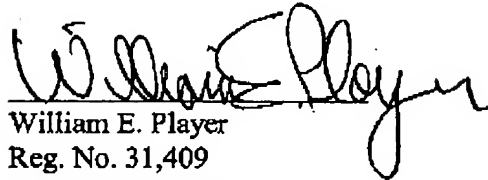
In view of the foregoing remarks, the rejection of claims 67-71, 76-80, 83-86, 88, 90, 91, 93-96 and 98 under 35 U.S.C. §103(a), as allegedly being unpatentable over Saito, Heid, GenBank sequence, Higashi, Stoll-Becker, Su and Buck, is overcome. Withdrawal of the rejection is in order.

Claims 100-103 and 105 were rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Saito as allegedly evidenced by Heid and GenBank sequence, Higashi, Stoll-Becker, Su, Buck, U.S. Patent No. 6,635,428 (Pasupuletti), and Stratagene Catalog. The rejection cannot be maintained for the same reasons (set forth above) with respect to the rejection of present claim 84, since rejected claims 100-103 and 105 are dependent (directly or indirectly) on present claim 84. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988). Withdrawal of the rejection is in order.

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Favorable action is requested.

Respectfully submitted,



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